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Efficacy and Feasibility of Behavioral Treatments for Migraine, Headache and Pain in the Acute Setting, Emergency Department and Urgent Care Settings

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Abstract

Purpose of review: This narrative review examines the use of behavioral interventions for acute treatment of headache and pain in the emergency department (ED)/urgent care (UC) and inpatient settings.

Recent findings: Behavioral interventions demonstrate reductions of pain and associated disability in headache, migraine and other conditions in the outpatient setting. Behavioral treatments may be a useful addition for patients presenting with acute pain to hospitals and emergency departments.

Summary: We review challenges, limitations, and offer suggestions for implementation of behavioral interventions in the acute setting. Some evidence exists for relaxation-based treatments, mindfulness-based treatments, hypnosis/self-hypnosis, and immersive virtual reality for acute pain, migraine and headache. There are few high-quality studies on behavioral treatments in the inpatient and emergency department settings. Further research is warranted to determine the efficacy and cost-effectiveness of these interventions. Given the general safety and cost

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effectiveness of behavioral interventions, healthcare professionals may want to include these therapies in treatment plans.

Keywords

Pain management; Non-pharmacologic; Behavioral; Cognitive behavioral therapy; Relaxation training; Biofeedback; Mindfulness

Introduction

Acute pain, headache and migraine are common reasons for presentations to emergency departments and for admissions to the hospital [1]. Medications and injection-based therapies are frequently used for acute pain management. Many of these therapeutics, while effective, carry risks of adverse events [2]. In addition, the overuse of opiates has led to a nation-wide epidemic of abuse, misuse and dependence in the US [3]. Behavioral interventions are not a standard part of inpatient or emergency department (ED)/ urgent care (UC) migraine, headache or pain treatment [2]. Nonetheless, the safety and efficacy of many behavioral treatments for pain and headache has been demonstrated convincingly in the outpatient setting [4]. This review discusses the application of behavioral treatments for treating acute inpatient pain.

The neurophysiology of acute pain differs from that of chronic pain [5]. Brain regions involved in acute pain include: the primary and secondary somatosensory cortex, the anterior cingulate cortex, the amygdala, the periaqueductal gray, the anterior insula, and the nucleus accumbens, the posterior insula, and the thalamus. In chronic pain, the medial prefrontal cortex has been shown to be the region which best-correlates with fluctuations of pain, and there is a reduced connectivity in tracts involved in descending pain modulation. Given these physiologic differences, there may be different levels of effectiveness of behavioral interventions for acute pain compared with chronic pain.

For the purposes of this review, we define behavioral therapies as non-pharmacologic therapies that rely on the patient's active behavioral participation. Some non-pharmacologic treatments (e.g. acupuncture, massage, transcutaneous electrical nerve stimulation) have been excluded from this review as they rely on physical effects rather than the patient's active behavioral participation.

Candidate behavioral interventions for use in acute pain, migraine and headache are reviewed in Table 1. In the next section, we will review the evidence base for these behavioral interventions in the outpatient setting. Then, we will review the evidence-base of these interventions for acute pain, migraine and headache. Finally, we will discuss practical issues in applying these modalities to the inpatient setting.

Evidence base in the outpatient setting

Many trials have studied behavioral treatments for migraine, other primary headache disorders, and chronic pain in the outpatient setting. Relaxation training, biofeedback and cognitive-behavioral therapy have strong evidence of effectiveness for migraine and tension-

type headache management [6]. These modalities have yielded 35 to 50% reductions in migraine, on par with the efficacy of traditional pharmacologic preventive treatments [4]. These therapies have also been shown to be effective when learned in a home-based setting. Haddock et al. [7] analyzed 20 trials of home-based behavioral treatments (including home-based relaxation treatments, biofeedback, and minimal therapist-contact CBT), and found them equally effective, or superior to, clinic-based interventions. Moreover, these home-based treatments were significantly more cost-effective.

The use of behavioral and pharmacologic therapies has been shown to be synergistic and effective in both adults and children. Holroyd et al. [8] performed a trial of 203 adults with chronic tension-type headache randomly assigned amitriptyline or nortriptyline vs. placebo vs. stress management therapy (relaxation and cognitive coping strategies taught over 3 face-to-face sessions and 2 telephone contacts) and found that pharmacotherapy was equally effective compared to behavioral therapy. Furthermore, the patients who received combined therapy were more likely to have clinically significant (>50%) reductions in headache index scores than either treatment alone.

Powers et al. [9] randomized 135 patients aged 10-17 with chronic migraine to amitriptyline + CBT or amitriptyline + headache education and found greater effects in the amitriptyline + CBT group. This is interesting especially in the context of the recently published CHAMP trial, where amitriptyline and topiramate, two medicines with high levels of evidence for episodic migraine prevention in adults [10], were found to be no more effective than placebo in children [11].

In contrast to the above well-established behavioral therapies for migraine, Acceptance and Commitment Therapy (ACT), mindfulness-based interventions (MBCT and MBSR), and sleep interventions are emerging as potentially effective migraine treatments, but more data is needed before these can be definitively recommended [12]. Two systematic reviews have assessed ACT vs. treatment as usual, and have found improvements in depressive symptoms, disability, affective perceptions of pain and anxiety [13, 14]. Similar results have been seen in several mindfulness based therapy trials for migraine and other severe headache. Most recently, Seng et al, 2019 adapted a migraine-specific form of MBCT (mindfulness-based cognitive therapy for migraine; MBCT-M). Results of this phase 2b randomized controlled clinical trial among people with migraine observed significant reductions in headache-related disability, but not a reduction in headache days or pain intensity in the active treatment group [15].

Table 2 summarizes the systematic reviews supporting behavioral interventions in chronic non-headache pain. Table 3 summarizes evidence grades for migraine, headache and chronic pain.

Evidence-base for behavioral treatments for pain and primary headache in the experimental and acute settings

Experimentally-induced pain

Pain can be induced in an experimental setting in healthy volunteers by applying a noxious stimulus (e.g. cold or electricity) without causing tissue damage. Though not perfectly analogous to acute pain in hospitalized patients, acute experimental pain provides a useful model to assess the efficacy of behavioral interventions. Here we review studies of behavioral treatments in experimentally-induced pain. Overall, these results do not show reduced pain intensity, but do show some secondary psychological benefits.

Several studies have investigated relaxation training in experimentally-induced pain. Smith and Norman [32] randomized 63 undergraduates to either a 10-minute deep breathing condition, a 10-minute progressive muscle relaxation condition or a control condition. The participants were then exposed to a cold pressor pain protocol. The authors found no statistically significant effects of this brief relaxation training on pain (Hazard Ratio = 0.991, $p = 0.962$). Juhasz et al. [33] induced headache with nitroglycerin and found that autogenic training, a type of relaxation training, was not effective in preventing nitroglycerin-induced migraine (8/16 vs. 14/25 immediate headaches in the treatment vs. control groups, $p=0.707$). Busch et al. [34] analyzed the effect of two types of deep and slow breathing on pain perception, autonomic activity, and mood processing in 16 healthy volunteers exposed to cold and hot pain stimuli. Both breathing interventions resulted in reduced total mood disturbances (range: 0-200 on the "Profile of Mood States" scale, before 9.87, 13.98 -> after 0.9, 3.04 for the attentive and relaxed breathing conditions, $P<0.5$, $P<0.01$).

Emery et al. [35] randomized 55 college students to a 25 minute progressive muscle relaxation (PMR) training or no treatment, and measured the nociception flexion response threshold (electrical stimulation was applied to the foot, and the current when the leg withdraws was recorded). First, both groups were tested in the experimental pain condition. Then one group ($n=28$) was taught PMR and was encouraged to apply it during the experimental pain situation. The other group ($n=27$) was not given specific instructions and were told to read, work or sit quietly for ~25 minutes. In the experimental group, the nociception flexion threshold increased ($p < 0.05$), and the measures of stress decreased ($p < 0.001$) while there was no change in the control group.

Esch et al. [36] randomized fifteen participants to no intervention vs. sixteen to a combined breathing/mindfulness meditation technique in five daily group sessions of 1.5 hours each for five days. Subjects were not told about how to use mindfulness for pain to avoid a placebo effect. The participants were then subjected to the tourniquet test (a blood pressure cuff is inflated over an arm, and time that the participant can withstand the ischemic pain is measured). This intervention did not reduce pain or improve pain tolerance (control group gained 5m 37s in the tourniquet test compared to the intervention group gaining only 2m 01s).

Petter [37] randomized 198 adolescents to a mindful attention manipulation or control group prior to an experimental pain task (the cold pressor task, in which the subject places their

hand in cold water and time submerged is measured). The authors found no effect on pain, but interestingly, regular meditators in the mindful attention group reported lower pain intensity than mediators in the control condition (mean pain score on a 10-point scale were 5 and 6.5, $p < 0.5$). In a follow-up study, Petter [38] randomized 82 children to mindful attention (attention towards pain) or guided imagery groups (attention away from pain). There were no differences in measures of pain intensity or pain tolerance.

Grant and Rainville [39] performed a cross-sectional study of pain perception in highly-trained Zen meditators (>1000 hours of practice) vs. controls. They found that the Zen meditators required higher temperatures to elicit moderate pain (meditators: 49.9°C; controls: 48.2°C; $p = 0.01$) and that the meditators could modulate the pain by attending “mindfully.”

Zeidan et al. [40] performed a study of mindfulness meditation versus several control conditions: a placebo cream, a sham mindfulness meditation (in which subjects were asked to sit without explicit instructions to focus on their breath), and listening to an audiobook. The aim in this study was to determine the mechanisms of action of mindfulness meditation by comparing it to other behavioral treatments. Mindfulness meditation decreased pain intensity by 27%, while placebo decreased intensity by 11%, sham mindfulness by 8 (p values < 0.05). Mindfulness meditation also decreased pain unpleasantness (by 44% in contrast to 27% in the sham mindfulness condition, p values < 0.05). On fMRI, the mindfulness meditation group was found to have different activity of multiple areas involved in the cognitive processing of pain (including activation of the orbitofrontal cortex, anterior cingulate cortex and deactivation of the thalamus) compared to each of the placebo conditions.

Grant [41] conducted a cross-sectional study in Zen meditators versus controls and found that during pain, meditators had stronger activity in regions typically associated with sensory and affective pain processing, and that meditators had reduced functional connectivity between the dorsolateral prefrontal cortex and anterior cingulate cortex where the degree of connectivity strongly predicted baseline pain sensitivity.

Many studies support the concept of “meditative analgesia” in long-term meditation practitioners who undergo experimental pain (reviewed in [42]). Across studies, long-term meditators have a higher pain tolerance and report pain stimuli as less unpleasant. On fMRI and EEG studies during the painful stimuli, different brain regions are activated in long-term meditators compared to controls. However it is unlikely that these benefits would be accessible to an individual without a long-term meditation practice.

Hypnosis has been compared to active control conditions in various types of experimental pain (see [29] for a meta-analysis of 17 studies). The data overall show a moderate-to-large effect size (Mean weighted effect size = 0.67) for hypnosis as an acute treatment for experimental pain.

Acute pain in surgical, post-operative, labor and delivery and inpatient settings

Behavioral treatments for acute pain have been used for hundreds of years. For example, prior to the advent of ether, hypnosis was used as the only anesthetic in some surgeries [43]. Yet despite this long history, the systematic study of behavioral interventions for acute pain through randomized trials is in its infancy.

Smith [44] reviewed eleven trials (1,374 women) and found that relaxation techniques and yoga may help manage labor pain, with some trials reporting less intense pain, increased satisfaction with pain relief / childbirth and lower rates of assisted vaginal delivery. However, no clinical recommendation was made due to methodological issues. Duncan [45] et al. conducted an RCT of mindfulness for childbirth, and found no difference in retrospective reports of labor pain or use of epidural anesthesia but found lower rates of depression, a trend towards using less opiates in labor, and greater self-efficacy and body awareness. In a small pilot study, Minen et. al. [46] enrolled patients presenting to the emergency department with migraine and found that progressive muscle relaxation was feasible in a brief period of time (typically less than 15 minutes), and most patients were agreeable to trying the intervention.

Ziehm et al. [47] reviewed the evidence for psychoeducation, cognitive restructuring, relaxation techniques in the reduction of pain after open-heart surgery, and found insufficient evidence to comment on the efficacy of these interventions for pain. The authors found moderate-quality evidence for these interventions in reducing mental distress. Seers and Carroll [48] reviewed 7 studies (362 patients) of relaxation techniques for acute postsurgical/postprocedural pain and found weak and inconclusive evidence that relaxation-based treatments are useful for acute pain, and poor methodological quality in the studies reviewed.

Garland [49] et al. ran a randomized-controlled trial of mindfulness for inpatient pain comparing mindfulness training vs. hypnotic suggestion vs. psychoeducation for acute pain relief in the hospital setting. Each of the interventions were brief (15 minutes in length) and administered by a hospital social worker. The mindfulness and hypnotic suggestion interventions consisted of scripted training sessions, and the psychoeducation group consisted of a meeting with a social worker and providing of behavioral coping strategies. The authors found that the single brief mindfulness or hypnotic suggestion intervention reduced pain more than the psychoeducation group. The authors found that approximately 30% of patients in these groups had a 30% reduction in pain, which they equated as being similar to 5mg oxycodone.

Ardigo [50] et al. randomized 53 hospitalized elderly patients to self-hypnosis vs. massage to assess the immediate and long-term effects of hypnosis in chronic pain at various sites (back pain, knee pain, neuropathic pain, shoulder pain, fibromyalgia, other). The authors found significantly reduced pain intensity in the hypnosis group compared to the massage group while the patients were hospitalized ($p = 0.008$). The effect was not sustained after discharge. Katz [51] et al. randomized children with acute lymphoblastic leukemia undergoing repeated bone marrow aspiration procedures to hypnosis or play intervention

groups and found the two equally effective in improving self-reported distress compared to baseline.

In contrast to most of the other modalities discussed in this paper, Immersive Virtual Reality (IVR) has more evidence for application to acute pain rather than chronic pain. Garrett et al. reviewed 5 RCTs, 6 randomized crossover studies, and 6 non-randomized studies (337 patients total) of IVR as an adjunct for the management of acute pain [52]. The authors found strong overall evidence for immediate and short-term pain reduction, with little evidence for long-term benefits, and no adverse events. A more recent review by Won et. al reviews the literature for IVR for pediatric pain relief and provides practical suggestions for inexpensive consumer-grade IVR hardware and software for the interested clinician [53].

IVR has been utilized in numerous acute pain settings such as bandage changes for severe burns, IV line placement, port access, and dental procedures [52, 54]. A recent randomized trial of IVR was conducted in hospitalized patients with a wide range of pain conditions. The trial compared IVR with a 2-D distraction video and found that 65% of the IVR patients achieved a pain response vs. 40% of patients in the control group ($P=0.1$, number needed to treat = 4) [54].

Discussion

Despite the evidence base for many behavioral treatments delivered or taught in the outpatient setting, more robust studies in the inpatient setting are needed before they become a routine part of inpatient pain treatment.

In our opinion, the ideal behavioral interventions for inpatient use would be simple to administer, brief and inexpensive. Such interventions would be easily teachable to a wide range of healthcare providers, and to patients for home use. They would require no sophisticated equipment and would have a rapid onset of action. The goals of behavioral treatments are similar to those of pharmacologic treatments: a reduction in pain, anxiety, reduced disability, improved quality of life, improved adherence, and reduced costs.

There is the question of efficacy with a single experience in an acute setting. Most behavioral interventions (e.g. biofeedback, relaxation, mindfulness, or stress management approaches) are taught and practiced over several sessions and become increasingly effective over periods of practice as patients gain competence in these methods and balance the nervous system. It remains to be determined if these interventions can be applied effectively in the inpatient setting where multiple sessions are often not possible and patients may have no prior experience with these techniques. Also, in the acute setting patients are typically having a much greater-than-baseline level of pain. It is not clear that interventions effective for outpatients will be useful for those in high levels of acute pain and distress.

A specific methodological challenge for trials of behavioral treatment is the choice of control group. Control groups can be *no treatment* (e.g. a waiting list control), *minimal treatment* (e.g. a very brief intervention), a *non-specific active control* (a condition in which no clear rationale for the treatment is provided), or a *specific active controls* (a condition where a clear rationale for the treatment is provided to the patient). In addition, a behavioral

treatment may be compared head-to-head with a widely accepted evidence-based treatment. The choice of control group matters when interpreting the results of studies. For example, in a recent meta-analysis of 171 randomized trials (12,005 patients) of mindfulness for psychiatric disorders and pain, the authors found that the relative effectiveness of mindfulness-based interventions varied based on the type of control groups used [55].

If efficacy is proven, the next obstacle to overcome is access to providers and resources. Ernst et al. [56] classified barriers to behavioral treatment for migraine into patient and provider-related. These treatments require patient buy-in, and will not work for patients uninterested in these treatments [6] or patients in too much pain to focus on the interventions. Even if patients attain success with the intervention, long-term adherence may be a challenge. As a case in point, the Adherence in Migraine (AIM) study assessed compliance with pharmacologic and behavioral intervention via an app [57]. The measured average number of cups of non-caffeinated fluid intake was 5 cups per day, below the recommendation (>8 cups per day). Participants also reported skipping 1 meal per week, despite recommendations of eating three meals per day.

On the provider-side, there needs to be individuals who are trained and proficient in administering behavioral treatments as well as able to bill for them. These modalities typically have inconsistent insurance reimbursement which may be limited to certain provider types, and this will likely limit the adoption of these modalities by health care systems and individual providers. Nonetheless, if efficacy for inpatient/ emergency department use is proven, more comprehensive reimbursement could be a future goal as these treatments are relatively inexpensive and will likely reduce associated healthcare resource utilization and costs.

The hospital setting itself may be a barrier to the use of some of these treatments. For instance, a loud and crowded emergency department is not the traditional environment for teaching relaxation techniques. In some cases, it may be possible to take a patient into a less stimulating treatment room of the ED to teach a behavioral intervention.

Within certain behavioral treatment modalities, provider skill may be a factor. There may be vast differences working with a psychologist or skilled meditation teacher in comparison to a paraprofessional, novice, a handout, or an electronic or web based resource. Further research will be needed to identify and/or develop empirically validated treatments that can be delivered using inexperienced providers or via low- or no-touch interventions.

Electronic and low-touch methods of teaching many behavioral interventions are also being developed to investigate more scalable methods of delivery of these behavioral interventions. The specific implementation of these treatments is changing rapidly with technology, especially with the ubiquity of smart phones and personal health tracking devices. At the time of a 2016 systematic review of electronic behavioral interventions for headache, there were over 40 headache apps in the Google Play store and over 70 in the U.S. Apple iTunes store [58]. The authors found 9 studies of electronic CBT interventions with N>30; there were positive outcomes in headache frequency, severity, and medication use in 4 of them. The authors found 7 studies of relaxation with N>30, and found only 2 of them to have

positive outcomes (decreased migraine frequency and peak intensity). There were even fewer studies of electronic biofeedback and only one with a positive result (decreased pain intensity).

Though research into behavioral treatments for acute pain is still in its infancy, it is ethical to trial these therapies if risks are deemed to be lower than potential benefits and the patient is interested.

Conclusion

A robust body of literature exists documenting the efficacy of diverse behavioral treatments for outpatient pain, migraine and headache management. There have been numerous studies on behavioral treatments for acute experimentally-induced pain, with evidence for mindfulness based therapies, relaxation, and hypnosis treatments. In comparison, there is a much smaller body of literature for the application of behavioral treatments to the management of headache, migraine and pain in acute inpatient or emergency department or urgent care settings. Some research supports the acute use of relaxation therapies, mindfulness based therapies, hypnosis, and virtual reality based delivery systems in these settings. These therapies can be led by professionals or self-guided by patients using psychoeducational and technological support. Use of these behavioral methods in the inpatient setting is ethical when benefits are thought to outweigh risks and the patient is interested.

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Abbreviations

MBSR	Mindfulness-based stress reduction
MBCT	Mindfulness-based cognitive therapy
ACT	Acceptance and Commitment therapy
CBT	Cognitive behavioral therapy

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Weiss AJ, et al., Overview of Emergency Department Visits in the United States, 2011: Statistical Brief #174, in Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. 2006: Rockville (MD).
2. Levin M, Approach to the Workup and Management of Headache in the Emergency Department and Inpatient Settings. *Semin Neurol*, 2015 35(6): p. 667–74. [PubMed: 26595867]

3. Dowell D, Haegerich TM, and Chou R, CDC Guideline for Prescribing Opioids for Chronic Pain-- United States, 2016. *JAMA*, 2016 315(15): p. 1624–45. [PubMed: 26977696]
4. Penzien DB, et al., Well-Established and Empirically Supported Behavioral Treatments for Migraine. *Curr Pain Headache Rep*, 2015 19(7): p. 34. [PubMed: 26065542]
5. Flor H, Psychological pain interventions and neurophysiology: implications for a mechanism-based approach. *Am Psychol*, 2014 69(2): p. 188–96. [PubMed: 24547804]
6. Nicholson RA, et al., Nonpharmacologic treatments for migraine and tension-type headache: how to choose and when to use. *Curr Treat Options Neurol*, 2011 13(1): p. 28–40. [PubMed: 21080124]
7. Haddock CK, et al., Home-based behavioral treatments for chronic benign headache: a meta-analysis of controlled trials. *Cephalalgia*, 1997 17(2): p. 113–8. [PubMed: 9137849]
8. Holroyd KA, et al., Management of chronic tension-type headache with tricyclic antidepressant medication, stress management therapy, and their combination: a randomized controlled trial. *JAMA*, 2001 285(17): p. 2208–15. [PubMed: 11325322]
9. Powers SW, et al., Cognitive behavioral therapy plus amitriptyline for chronic migraine in children and adolescents: a randomized clinical trial. *JAMA*, 2013 310(24): p. 2622–30. [PubMed: 24368463]
10. Loder E, Burch R, and Rizzoli P, The 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. *Headache*, 2012 52(6): p. 930–45. [PubMed: 22671714]
11. Powers SW, et al., Trial of Amitriptyline, Topiramate, and Placebo for Pediatric Migraine. *N Engl J Med*, 2017 376(2): p. 115–124. [PubMed: 27788026]
12. Smitherman TA, Wells RE, and Ford SG, Emerging behavioral treatments for migraine. *Curr Pain Headache Rep*, 2015 19(4): p. 13. [PubMed: 25819975]
13. Veehof MM, et al., Acceptance- and mindfulness-based interventions for the treatment of chronic pain: a meta-analytic review. *Cogn Behav Ther*, 2016 45(1): p. 5–31. [PubMed: 26818413]
14. Hughes LS, et al., Acceptance and Commitment Therapy (ACT) for Chronic Pain: A Systematic Review and Meta-Analyses. *Clin J Pain*, 2017 33(6): p. 552–568. [PubMed: 27479642]
15. Seng E, Singer AB, Metts C, Does Mindfulness-based cognitive therapy for migraine reduce migraine-related disability in people with episodic and chronic migraine? A phase 2b pilot randomized clinical trial. *Headache*, 2019.
16. Williams AC, Eccleston C, and Morley S, Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database Syst Rev*, 2012 11: p. CD007407. [PubMed: 23152245]
17. Henschke N, et al., Behavioural treatment for chronic low-back pain. *Cochrane Database Syst Rev*, 2010(7): p. CD002014. [PubMed: 20614428]
18. Monticone M, et al., Cognitive-behavioural treatment for subacute and chronic neck pain. *Cochrane Database Syst Rev*, 2015(5): p. CD010664. [PubMed: 26006174]
19. Fisher E, et al., Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev*, 2015(3): p. CD011118. [PubMed: 25803793]
20. Eccleston C, et al., Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev*, 2014(5): p. CD003968. [PubMed: 24796681]
21. Abbott RA, et al., Psychosocial interventions for recurrent abdominal pain in childhood. *Cochrane Database Syst Rev*, 2017 1: p. CD010971. [PubMed: 28072460]
22. Adachi T, et al., A meta-analysis of hypnosis for chronic pain problems: a comparison between hypnosis, standard care, and other psychological interventions. *Int J Clin Exp Hypn*, 2014 62(1): p. 1–28. [PubMed: 24256477]
23. Sielski R, Rief W, and Glombiewski JA, Efficacy of Biofeedback in Chronic back Pain: a Meta-Analysis. *Int J Behav Med*, 2017 24(1): p. 25–41. [PubMed: 27307013]
24. Chou R, et al., Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*, 2007 147(7): p. 478–91. [PubMed: 17909209]

25. Fisher E, et al., Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev*, 2014 2014.
26. Flynn N, Systematic Review of the Effectiveness of Hypnosis for the Management of Headache. *Int J Clin Exp Hypn*, 2018 66(4): p. 343–352. [PubMed: 30152733]
27. Hammond DC, Review of the efficacy of clinical hypnosis with headaches and migraines. *Int J Clin Exp Hypn*, 2007 55(2): p. 207–19. [PubMed: 17365074]
28. Abbott RA, et al., Recurrent Abdominal Pain in Children: Summary Evidence From 3 Systematic Reviews of Treatment Effectiveness. *J Pediatr Gastroenterol Nutr*, 2018.
29. Montgomery GH, DuHamel KN, and Redd WH, A meta-analysis of hypnotically induced analgesia: how effective is hypnosis? *Int J Clin Exp Hypn*, 2000 48(2): p. 138–53. [PubMed: 10769981]
30. Yang CP and Wang SJ, Sleep in Patients with Chronic Migraine. *Curr Pain Headache Rep*, 2017 21(9): p. 39. [PubMed: 28785964]
31. Cheattle MD, et al., Assessing and Managing Sleep Disturbance in Patients with Chronic Pain. *Sleep Med Clin*, 2016 11(4): p. 531–541. [PubMed: 28118876]
32. Smith KE and Norman GJ, Brief relaxation training is not sufficient to alter tolerance to experimental pain in novices. *PLoS One*, 2017 12(5): p. e0177228. [PubMed: 28493923]
33. Juhasz G, et al., Effects of autogenic training on nitroglycerin-induced headaches. *Headache*, 2007 47(3): p. 371–83. [PubMed: 17371354]
34. Busch V, et al., The effect of deep and slow breathing on pain perception, autonomic activity, and mood processing--an experimental study. *Pain Med*, 2012 13(2): p. 215–28. [PubMed: 21939499]
35. Emery CF, et al., Effects of progressive muscle relaxation training on nociceptive flexion reflex threshold in healthy young adults: a randomized trial. *Pain*, 2008 138(2): p. 375–9. [PubMed: 18291584]
36. Esch T, et al., Neurobiological Aspects of Mindfulness in Pain Autoregulation: Unexpected Results from a Randomized-Controlled Trial and Possible Implications for Meditation Research. *Front Hum Neurosci*, 2016 10: p. 674. [PubMed: 28184192]
37. Petter M, et al., The effects of mindful attention and state mindfulness on acute experimental pain among adolescents. *J Pediatr Psychol*, 2014 39(5): p. 521–31. [PubMed: 24599947]
38. Petter M, Chambers CT, and MacLaren Chorney J, The effects of mindfulness-based attention on cold pressor pain in children. *Pain Res Manag*, 2013 18(1): p. 39–45. [PubMed: 23457685]
39. Grant JA and Rainville P, Pain sensitivity and analgesic effects of mindful states in Zen meditators: a cross-sectional study. *Psychosom Med*, 2009 71(1): p. 106–14. [PubMed: 19073756]
40. Zeidan F, et al., Mindfulness Meditation-Based Pain Relief Employs Different Neural Mechanisms Than Placebo and Sham Mindfulness Meditation-Induced Analgesia. *J Neurosci*, 2015 35(46): p. 15307–25. [PubMed: 26586819]
41. Grant JA, Courtemanche J, and Rainville P, A non-elaborative mental stance and decoupling of executive and pain-related cortices predicts low pain sensitivity in Zen meditators. *Pain*, 2011 152(1): p. 150–6. [PubMed: 21055874]
42. Grant JA, Meditative analgesia: the current state of the field. *Ann N Y Acad Sci*, 2014 1307: p. 55–63. [PubMed: 24673150]
43. Schuyler BS, et al., Temporal dynamics of emotional responding: amygdala recovery predicts emotional traits. *Soc Cogn Affect Neurosci*, 2014 9(2): p. 176–81. [PubMed: 23160815]
44. Smith CA, et al., Acupuncture or acupressure for pain management in labour. *Cochrane Database Syst Rev*, 2011(7): p. CD009232. [PubMed: 21735441]
45. Duncan LG, et al., Benefits of preparing for childbirth with mindfulness training: a randomized controlled trial with active comparison. *BMC Pregnancy Childbirth*, 2017 17(1): p. 140. [PubMed: 28499376]
46. Minen M, et al., Introduction to Progressive Muscle Relaxation Therapy for Migraine in the Emergency Department: A Pilot Feasibility Study (P2.168). *Neurology*, 2017 88(16 Supplement).
47. Ziehm S, et al., Psychological interventions for acute pain after open heart surgery. *Cochrane Database Syst Rev*, 2017 7: p. CD009984. [PubMed: 28701028]

48. Seers K and Carroll D, Relaxation techniques for acute pain management: a systematic review. *J Adv Nurs*, 1998 27(3): p. 466–75. [PubMed: 9543031]
- 49••. Garland EL, et al., Randomized Controlled Trial of Brief Mindfulness Training and Hypnotic Suggestion for Acute Pain Relief in the Hospital Setting. *J Gen Intern Med*, 2017 32(10): p. 1106–1113. [PubMed: 28702870]
- 50•. Ardigo S, et al., Hypnosis can reduce pain in hospitalized older patients: a randomized controlled study. *BMC Geriatr*, 2016 16: p. 14. [PubMed: 26767506]
51. Katz ER, Kellerman J, and Ellenberg L, Hypnosis in the reduction of acute pain and distress in children with cancer. *J Pediatr Psychol*, 1987 12(3): p. 379–94. [PubMed: 3479547]
52. Garrett B, et al., A rapid evidence assessment of immersive virtual reality as an adjunct therapy in acute pain management in clinical practice. *Clin J Pain*, 2014 30(12): p. 1089–98. [PubMed: 24535053]
- 53••. Won AS, et al., Immersive Virtual Reality for Pediatric Pain. *Children (Basel)*, 2017 4(7).
- 54••. Tashjian VC, et al., Virtual Reality for Management of Pain in Hospitalized Patients: Results of a Controlled Trial. *JMIR Ment Health*, 2017 4(1): p. e9. [PubMed: 28356241]
55. Goldberg SB, et al., Mindfulness-based interventions for psychiatric disorders: A systematic review and meta-analysis. *Clin Psychol Rev*, 2018 59: p. 52–60. [PubMed: 29126747]
56. Ernst MM, O'Brien HL, and Powers SW, Cognitive-Behavioral Therapy: How Medical Providers Can Increase Patient and Family Openness and Access to Evidence-Based Multimodal Therapy for Pediatric Migraine. *Headache*, 2015 55(10): p. 1382–96. [PubMed: 26198185]
57. Kroon Van Diest AM, et al., Adherence to Biobehavioral Recommendations in Pediatric Migraine as Measured by Electronic Monitoring: The Adherence in Migraine (AIM) Study. *Headache*, 2016 56(7): p. 1137–46. [PubMed: 27167502]
58. Minen MT, et al., Electronic behavioral interventions for headache: a systematic review. *J Headache Pain*, 2016 17: p. 51. [PubMed: 27160107]

Table 2.

Systematic reviews and meta analyses of behavioral interventions in chronic non-headache pain

Authors	Type of pain	Intervention	Number of trials (number of participants)	Standardized effect sizes (in standard deviation (SD) units) post-treatment
Williams et al. [16]	Chronic non-headache pain	Behavioral therapy, CBT, biofeedback	35 RCTs (4,788 participants)	- Small positive effects of CBT on disability (−0.19 SD) and catastrophizing (−0.18 SD), but not pain or mood when compared to active controls - Small to moderate effects on pain (−0.21 SD), disability (−0.26 SD), mood (−0.38 SD) and catastrophizing (−0.53 SD) compared to treatment-as-usual/waiting list controls
Henschke et al. [17]	Low-back pain	Progressive muscle relaxation, biofeedback, various psychotherapies (CBT, operant therapy, combined behavioral therapy)	30 RCTs (3,438 total patients)	Compared to waiting-list controls: -Progressive muscle relaxation had benefits on functional status (−0.88 SD), but not pain or depression -EMG biofeedback had benefits on pain (−0.80 SD) but not functional status -Operant therapy and CBC had benefits on pain (−0.43 and −0.60 SD, respectively) but not functional status or depression
Monticone et al. [18]	Subacute and chronic neck pain	CBT	10 RCTs (836 patients)	- CBT more effective than no treatment for chronic neck pain (−0.58 SD)
Fisher et al. [19] Eccleston et al. [20]	Chronic and recurrent headache and non-headache pain in children and adolescents	Psychological treatments (relaxation, hypnosis, coping skills training, biofeedback, CBT) delivered remotely (Fischer et al.) or face-to-face (Eccleston et al.)	Fischer: 8 RCTs (371 children/adolescents) Eccleston: 37 RCTs (2,111 participants)	- Fischer et al.: Reduced pain but not disability (all psychological treatments and control types were combined in the analysis; −0.61 SD) - Eccleston et al.: For headache, psychological treatments reduce pain intensity (2.47 risk ratio), disability (−0.49 SD), and anxiety (−0.33 SD). For non-headache pain, these treatments reduce pain (−0.57 SD) and disability (−0.45 SD).
Abbott et al. [21]	Recurrent abdominal pain (without an organic cause) in children.	CBT, hypnotherapy (including guided imagery), yoga, written self-disclosure	18 RCTs (928 children/adolescents)	- CBT (−0.92 SD) and hypnosis (−1.00 SD) were effective in reducing pain (but only when compared to wait-list control for CBT) - No benefit for yoga therapy or written self-disclosure therapy
Veehof et al. [13]	Chronic headache and pain	Acceptance and commitment therapy (ACT) and mindfulness-based therapies	25 RCTs (1,285 subjects)	- Moderate effects on anxiety (−0.51 SD) and pain interference (0.62 SD) with activities - Small effects on pain intensity (−0.24 SD), depression (−0.43 SD), disability (−0.40 SD), quality of life (−0.44 SD)
Hughes et al. [14]	Chronic non-headache and non-cancer pain	Acceptance and commitment therapy (ACT)	11 RCTs (863 participants)	- Medium to large effect on acceptance (0.84 SD) and functioning (0.70 SD), small to medium effect on depression (−0.35 SD), no effect on pain intensity, anxiety or quality of life (compared to a relaxation active control group)
Adachi et al. [22]	Chronic pain and headache	Hypnosis	12 RCTs (933 participants)	- Moderately improved treatment efficacy for chronic pain compared to standard care (0.60 SD)
Sielski et al. [23]	Chronic back pain	Biofeedback	21 RCTs (1062 participants)	- Small-to-medium effect on pain intensity reduction (0.60 SD), depression reduction (0.40 SD), disability reduction (0.49 SD), muscle tension reduction (0.44 SD), and improved cognitive coping (0.41 SD)

Table 3 –

Evidence for behavioral treatments in migraine, headache and chronic pain

Behavioral Therapy	Evidence for migraine/ headache	Evidence for chronic pain
Relaxation-based therapies	Class I evidence for migraine and tension-type headache prophylaxis [6]. *	Grade B evidence for progressive muscle relaxation in chronic low back pain [24] **
Mindfulness-based therapies	Emerging evidence of some benefits, but not definitively effective [12] [15].	Benefit for pain, depression, anxiety and pain interference with daily activities [13, 15]
Cognitive Behavioral Therapy (CBT)	Class I evidence for migraine and tension headache management [6]. *	Effective for chronic pain in children and adults based on meta-analyses [16, 20, 25]. Grade B recommendation for low back pain [24] **
Hypnosis / Self-hypnosis	Several RCTs demonstrating decrease in headache frequency, intensity, mood, and quality of life; however, methodological quality is low [26] [27]	Benefit in recurrent abdominal pain in children [28] and a variety of chronic and experimental pain conditions [22, 29] based on meta-analyses.
Biofeedback	Class I evidence for migraine and tension headache [6]. *	Effective for chronic low back pain based on a recent meta-analysis [23].
Sleep interventions	Sleep interventions showed benefit in two small trials of chronic migraine [30].	CBTi for insomnia improved sleep, pain interference, fatigue and depression in small studies [31].

* Evidence class is from US Headache Consortium, Duke University's Center for Clinical Health Policy Research reviews

** Evidence from American Pain Society Guidelines [24]